Paper No. 39

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte AKIHIKO MARUYAMA,
TATSURO FUJIO, and SADAO TESHIBA

Appeal No. 1997-1307
Application No. 08/014,012

HEARD: October 10, 2000

Before WINTERS, ROBINSON, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 15-18 and 20-24 all the claims pending in the application. Claims 1-9 were canceled in appellants' amendment and response under 37 C.F.R. § 1.111.[1] Claims 10-14 and 19 were canceled, and claims 23 and 24 were added in appellants' amendment under 37 C.F.R. § 1.116.[2] These amendments were entered into the record. However, appellants' amendments under 37 C.F.R. § 1.193(b)[3] were not entered into the record.

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[1] January 28, 1994, Paper No. 14.
[2] November 2, 1994, Paper No. 19.
[3] Filed June 28, 1995, Paper No. 25, and November 20, 1995, Paper No. 30.

Claim 23 is illustrative of the subject matter on appeal and is reproduced below:

> 23. A process for producing cytidine diphosphate choline, which comprises contacting an enzymatically active treatment product of a culture of a microorganism which carries a recombinant DNA comprising a DNA fragment containing genes encoding pyrG, CCT and CKI and a vector (hereinafter referred to as Microorganism A1) and an enzymatically active treatment product of a culture of another microorganism which has orotate phosphoribosyltransferase, OMP decarboxylase, nucleosidemonophosphate kinase and nucleosidediphosphate kinase activities (hereinafter referred to as Microorganism B) with orotic acid and choline in a liquid medium; allowing cytidine diphosphate choline to accumulate in the liquid medium; and recovering cytidine diphosphate choline from the liquid medium.

Claim 24 is substantially the same as claim 23 with two exceptions: (1) Microorganism A1 is renamed Microorganism A2 and is not required to contain the gene encoding CKI, and (2) "phosphorylcholine" is "in the liquid medium" instead of "choline."

The references relied upon by the examiner are:

Gennari 4,789,666 Dec. 6, 1988

Weng et al. (Weng), "Nucleotide Sequence of *Escherichia coli pyrG* Encoding CTP Synthetase," J. Biol. Chem., Vol. 261, No. 12, pp. 5568-5574 (1986)

Neuhard et. al. (Neuhard), Purines and Pyrimidines, in 1 Escherichia coli and Salmonella Typhimurium: Cellular and Molecular Biology 445-473 (Frederick C. Neidhardt et al., eds., 1987)

Hosaka et al. (Hosaka), "Cloning and Characterization of the Yeast *CKI* Gene Encoding Choline Kinase and Its Expression in *Escherichia coli*," J. Biol. Chem., Vol. 264, No. 4, pp. 2053-2059 (1989)

Nudler et al. (Nudler), "The derepression of enzymes of de novo pyrimidine biosynthesis pathway in *Brevibacterium ammoniagenes* producing uridine-5-monophosphate and uracil, FEMS Microbiology Letters, Vol. 82, pp. 263-266 (1991)

Tsukagoshi et al. (Tsukagoshi), "Expression in *Escherichia coli* of the *Saccharomyces cerevisiae CCT* Gene Encoding Cholinephosphate Cytidylyltransferase," J. Bacteriology, Vol. 173, No. 6, pp. 2134-2136 (1991)

Sigma Chemical Company (SIGMA), 1992 Catalog, pp. 255, 302, 746-747, 811, 1009, 1011 and 1012 (1992)

GROUND OF REJECTION[4]

Claims 15-18 and 20-24 are rejected under 35 U.S.C. § 103 as being unpatentable over the combined teachings of Tsukagoshi, Weng and Hosaka, taken in view of Gennari, Nudler and SIGMA.

We reverse.

DISCUSSION

In reaching our decision in this appeal, we have given careful consideration to the appellants' specification and claims, and to the respective positions articulated by the appellants and the examiner. We make reference to the examiner's Answer[5], Supplemental Answer[6], and Second Supplemental Answer[7] for the examiner's reasoning in support of the rejection. We further reference appellants' Brief[8], Reply Brief[9], and Second Reply Brief[10] for the appellants' arguments in favor of patentability. Appellants' Reply Briefs received November 20,

[4] All grounds of rejection prior to the examiner's Supplemental Answer were withdrawn from consideration.
[5] Paper No. 23, mailed April 28, 1995.
[6] Paper No. 27, mailed September 20, 1995.
[7] Paper No. 34, mailed April 30, 1996.
[8] Paper No. 22, received January 3, 1995.
[9] Paper No. 26, received June 28, 1995.
[10] Paper No. 33, received February 28, 1996.

1995 (Paper No. 31) and July 1, 1996 (Paper No. 35) were not entered into the record, and therefore will not be relied upon for our decision.

THE REJECTION UNDER 35 U.S.C. § 103:

The examiner applies Weng, Hosaka and Tsukagoshi for their respective teaching of the cloning and expression of the pyrG, CKI, and CCT genes. While the examiner acknowledges that no reference suggests a recombinant DNA comprising pyrG and CCT (claim 24), or pyrG, CKI and CCT (claim 23), the examiner suggests that "[i]t would have been obvious … to combine the cloned genes … in order to construct a biosynthetic pathway to produce CDP-choline" (Answer[11], page 8). The examiner argues (Answer, page 9) that the "[m]otivation to combine the references is provided by Gennari who teaches that CDP-choline has therapeutic use in treating cerebral hemorrhages and cerebral thromboses…"

The examiner acknowledges (Answer, page 9) that the combination of Weng, Hosaka, Tsukagoshi and Gennari "do not teach or suggest co-culturing two strains or species of microorganisms to produce CDP-choline." The examiner argues (Answer, page 9) that "[t]his aspect of the claimed processes, however, is suggested by Nudler et al." While recognizing that Nudler "do not disclose the UTP-producing properties of their mutant strain" (Answer, page 10) which are specifically required in the claimed process, the examiner emphasizes that Nudler's microorganism produces UMP levels in the fermentation medium of up to 4 mg/ml.

[11] The examiner makes a new Ground of rejection in the Supplemental Answer and states (Supplemental Answer, page 3) "[t]his rejection is explained in the [e]xaminer's Answer to appellants' brief on appeal."

The examiner speculates (Answer, page 10) that "the skilled artisan would recognize that the conversion of UMP to UTP is essential for cell viability and the skilled artisan would therefore reasonably expect the cells to produce the enzymes for converting UMP to UDP … and for converting UDP to UTP." The examiner refers to SIGMA (Answer, page 12) to emphasize the purchase price of orotic acid, OMP, UMP, UDP, UTP, and CTP.

The examiner concludes (Answer, page 10) that:

> A person of ordinary skill … would have been motivated to combine the C. ammoniagenes strain taught by Nudler et al. with the recombinant E. coli taught by the combination of Weng et al., Hosaka et al., Tsukagoshi et al. and Gennari because the skilled artisan would realize that the UMP produced in large amounts by the C. ammoniagenes strain of Nudler et al. is a substrate in the synthesis of UTP, which is converted to CTP by the recombinant CTP synthetase enzyme.

To establish a prima facie case of obviousness, there must be more than the demonstrated existence of all of the components of the claimed subject matter. There must be some reason, suggestion, or motivation found in the prior art whereby a person of ordinary skill in the field of the invention would make the substitutions required. That knowledge cannot come from the applicants' disclosure of the invention itself. Diversitech Corp. v. Century Steps, Inc., 850 F.2d 675, 678-79, 7 USPQ2d 1315, 1318 (Fed. Cir. 1988); In re Geiger, 815 F.2d 686, 688, 2 USPQ2d 1276, 1278 (Fed. Cir. 1987); Interconnect Planning Corp. v. Feil, 774 F.2d 1132, 1143, 227 USPQ 543, 551 (Fed. Cir. 1985). On the record before us, we find no reasonable suggestion for combining the teachings of

the references relied upon by the examiner in a manner which would have reasonably led one of ordinary skill in this art to arrive at the claimed invention. The suggestion that CDP-choline is therapeutically useful and that a C. ammoniagenes overproduces UMP is, in our opinion, insufficient to suggest to a person of ordinary skill in the art to obtain a microorganism which carries a recombinant DNA comprising a DNA fragment containing genes encoding pyrG, CCT with or without CKI, and then culture this microorganism in the presence of a second microorganism which produces UTP.

The initial burden of presenting a prima facie case of obviousness rests on the examiner. In re Oetiker, 977 F.2d 1443, 1445, 24 USPQ2d 1443, 1444 (Fed. Cir. 1992). On these circumstances, we are constrained to reach the conclusion that the examiner has failed to meet his burden of establishing a prima facie case of obviousness. Instead, in this case the examiner has merely demonstrated the existence of all of the components of the claimed subject matter. What is missing is the requisite suggestion to combine the individual components to achieve the claimed invention.

In addition, we note that the examiner relies upon Neuhard (See e.g., Answer, page 6). However, Neuhard is not part of the examiner's statement of the rejection. We remind the examiner that "[w]here a reference is relied on to support a rejection, whether or not in a 'minor capacity,' there would appear to be no excuse for not positively including the reference in the statement of the rejection." In re Hoch, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n.3 (CCPA 1970).

Where the examiner fails to establish a prima facie case, the rejection is improper and will be overturned. In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). Accordingly, we reverse the examiner's rejection of claims 15-18 and 20-24 are rejected under 35 U.S.C. § 103 as being unpatentable over the combined teachings of Tsukagoshi, Weng and Hosaka, taken in view of Gennari, Nudler and SIGMA.

Having determined that the examiner has not established a prima facie case of obviousness, we find it unnecessary to discuss appellants' arguments regarding unexpected results.

REVERSED

Sherman D. Winters	)
Administrative Patent Judge	)
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	)
	) BOARD OF PATENT
Douglas W. Robinson	)
Administrative Patent Judge	) APPEALS AND
	)
	) INTERFERENCES
	)
Donald E. Adams	)
Administrative Patent Judge	)

DA/dm

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